REMARKS

Claims 45-54 are pending. Applicants make these amendments without prejudice to pursuing the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject mattered. Support for these amendments appears throughout the specification and claims as filed. No new matter is introduced by these amendments.

Rejection under 35 U.S.C. § 103(a)

Claims 45-54 are rejected as unpatentable over Herron (US Patent 4,764,521) in view of Rubenstein (IDS, CJ) and Wechter et al. (US Patent 5,981,592). Applicants traverse.

It is stated is in the Action that Herron generally teaches that substituted carboxylic acids are known to be useful for treating respiratory disease, including cystic fibrosis. While acknowledging that Herron does not teach Applicants' unsubstituted compound subject matter, it is further asserted in the Action that the teachings of Rubenstein and Wechter (both to unsubstituted aryl carboxylic acids) bridges the gap between Herron and Applicants' claimed subject matter. These assertions are sweeping, and the resulting conclusion on which they are based is an overbroad misinterpretation.

First, Herron does not definitively teach that Herron's compounds are useful in treating cystic fibrosis. A closer inspection of Herron shows that Herron: (i) describes their compounds as leukotriene antagonists (at col. 1, lines 18-22); (ii) notes that leukotrienes have been reported in sputum of cystic fibrosis patients (at col. 17, lines 47-51); (iii) postulates that this finding "suggests" a role of leukotrienes in cystic fibrosis (at col. 17, lines 52-53); and (iv) then concludes that the Herron compounds "should" also alleviate some of the symptoms of cystic fibrosis by virtue of their leukotriene antagonizing ability (at col. 17, lines 59-63). The combination of (i) to (iv) above incorporates much speculation

and fails to provide a reasonable basis for concluding with any degree of certainty that Herron teaches compounds useful in treating cystic fibrosis. Thus, Applicants traverse the assertion that Herron, in fact, teaches compounds that are established as useful in treating cystic fibrosis. As such, any combination with Herron is improper and fails to create a *prima facie* case of obviousness.

Applicant also traverse the asserted teachings of Rubenstein and Wechter in support of a *prima facie* case of obviousness. It is asserted that Wechter teaches aryl carboxylic acids known to be useful in treating cystic fibrosis. Again, this is an overbroad interpretation of Wechter. A closer inspection of Wechter indicates that Wechter, in fact, teaches the use of certain non-steroidal anti-inflammatory drugs (NSAIDs) for treating cystic fibrosis. However, the NSAIDS described by Wechter are all α-cyclic substituted acetic acid derivatives, and in fact, the positioning of the cyclic group at the α -position of the acetic acid is a required element. Applicants' claimed subject matter are not α -cyclic-substituted acetic acid compounds. Applicants' claimed compounds are distinct and distinguishable from Wechter in that Applicants' compounds are not α -substituted and not acetic acid compounds. Thus, Applicants submit that one of ordinary skill in the art, reading Wechter, would not be motivated to arrive at Applicants' claimed compounds for treating cystic fibrosis. There is no teaching or suggestion of Applicants' compound structures.

Similarly, Rubenstein teaches one compound, 4-phenylbutyric acid, for treatment of cystic fibrosis. Rubenstein, neither alone or in combination, provides any mention regarding Applicants' Δ3-trans-butenoic acid compound. The Rubenstein 4-phenylbutyric acid compound has a fully saturated hydrocarbon chain linking the acid and phenyl moleties. This is distinct and distinguishable from Applicants' Δ3-trans-butenoic acid compound, which has an unsaturated hydrocarbon chain. The physicochemical (including atom orbital geometry (i.e., sp2 v sp3 hybridization), three-dimensional spatial orientation, and thus functional properties (e.g. biological activity) and therapeutic properties of compounds having the carbon-carbon single bond (i.e., Rubenstein compound) are distinct

and distinguishable from compounds having the carbon-carbon double bond (i.e., Applicants' claimed subject matter). Rubenstein does not indicate any particular correlation between functional group moiety and cystic fibrosis activity of their compound, and on this basis Applicants submit that Rubenstein does not teach or suggest to one of ordinary skill in the art that Applicants' claimed carbon-carbon double bond containing compounds would necessarily be useful in treating cystic fibrosis. It is only Applicants' disclosure in their instant specification that provides such teaching. Applicants' therefore submit that a prima facie case is not made out and respectfully request that the rejection be withdrawn.

Nonetheless, Applicants submit that their claimed subject matter has unexpectedly superior activity relative to cited art compounds cinnamic acid and 4-PBA. Exhibit A (attached) is an autoradiograph showing ΔF508-CFTR protein expression in model cells of cystic fibrosis treated with the indicated compounds. ΔF508-CFTR is present in two bands, B and C. Band B corresponds to the immature core-glycosylated isoform of CFTR; Band C corresponds to the mature complex-glycosylated CFTR isoform. ΔF508-CFTR Bands Band C were quantitated by densitometry, and the quantitation is shown in Exhibit B (attached). Cells treated with trans-SAA produced increased amounts of both the immature and the mature forms of ΔF508-CFTR, consistent with an increase in CFTR production. These results indicate that trans-SAA is surprisingly effective in promoting the trafficking of functional ΔF508-CFTR to the cell surface relative to cinnamic acid and 4-PBA. Applicants therefore submit that their instantly claimed subject matter is not rendered obvious in view of the cited art and respectfully request withdrawal of the rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. (71699) 49632.

Dated: September 8, 2005

Respectfully submitted,

By _____

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Attachments